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The Biotechnology Systems Branch of the Scientific and Technical Information
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form:

Application Serial Number: 10/677,977A
Source: 1FW16
Date Processed by STIC: 9/30/05

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:
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FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT
MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE <u>CHECKER
VERSION 4.2.2 PROGRAM</u>, ACCESSIBLE THROUGH THE U.S. PATENT AND
TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:
   http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is
a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.
Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.
Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the
United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses.

1. EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm> , EFS Submission
   User Manual - ePAVE)
2. U.S. Postal Service: Commissioner for Patents. P.O. Box 1450, Alexandria, VA 22313-1450
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   U.S. Patent and Trademark Office, Mail Stop Sequence. Customer Window, Randolph Building. 401 Dulany Street.
   Alexandria. VA 22314

Revised 01/24/05
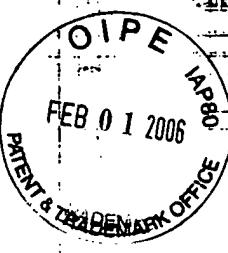
Raw Sequence Listing Error Summary

ERROR DETECTED	SUGGESTED CORRECTION	SERIAL NUMBER: 10/677,977A

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

1____Wrapped Nucleics The number/text at the end of each line "wrapped" down to the next line. This may occur if your file
     Wrapped Aminos   was retrieved in a word processor after creating it. Please adjust your right margin to 3. this will
    prevent "wrapping."

2____Invalid Line Length The rules require that a line not exceed 72 characters in length. This includes white spaces.

3____Misaligned Amino The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers:
    Numbering   use space characters, instead.

4____Non-ASCII The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. **Please
ensure your subsequent submission is saved in ASCII text.**

5____Variable Length Sequence(s)____contain n's or Xaa's representing more than one residue. **Per Sequence Rules,
each n or Xaa can only represent a single residue.** Please present the maximum number of each
residue having variable length and indicate in the <220>-<223> section that some may be missing.

6____PatentIn 2.0 A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid
    "bug"   sequences(s) _____. Normally, PatentIn would automatically generate this section from the
previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to
the subsequent amino acid sequence. **This applies to the mandatory <220>-<223> sections for
Artificial or Unknown sequences.**

7____Skipped Sequences Sequence(s) _____ missing. If intentional, please insert the following lines for each skipped sequence:
    (OLD RULES)   (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
    (i)   SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)
    (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
    This sequence is intentionally skipped

    Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.

8____Skipped Sequences Sequence(s) _____ missing. **If intentional, please insert the following lines for each skipped sequence.**
    (NEW RULES)   <210> sequence id number
    <400> sequence id number
    000

9____Use of n's or Xaa's Use of n's and/or Xaa's have been detected in the Sequence Listing.
    (NEW RULES)   Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present.
    In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.

10____Invalid <213> Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or
    Response   scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or
is Artificial Sequence

11____Use of <220> Sequence(s) _____ missing the <220> "Feature" and associated numeric identifiers and responses.
Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or
"Unknown." Please explain source of genetic material in <220> to <223> section.
(See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)

12____PatentIn 2.0 Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file,
    "bug"   resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence
listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.

13____Misuse of n/Xaa "n" can only represent a single <u>nucleotide</u>; "Xaa" can only represent a single <u>amino acid</u>
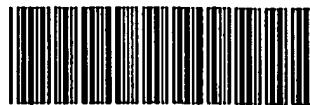
RAW SEQUENCE LISTING   DATE: 09/30/2005
PATENT APPLICATION: US/10/677,977A   TIME: 12:09:27

Input Set : A:\25840-501.txt
Output Set: N:\CRF4\09302005\J677977A.raw

```
 3 <110> APPLICANT: Nguyen, Jack
 4        Thanos, Chris
 5        Waugh Ruggles, Sandra
 6        Craik, Charles S.
 8 <120> TITLE OF INVENTION: METHODS OF GENERATING AND SCREENING FOR PROTEASES WITH
ALTERED
 9        SPECIFICITY
11 <130> FILE REFERENCE: 25840-501
13 <140> CURRENT APPLICATION NUMBER: 10/677,977A
14 <141> CURRENT FILING DATE: 2003-10-02
16 <150> PRIOR APPLICATION NUMBER: 60/425,388
17 <151> PRIOR FILING DATE: 2002-10-02
19 <160> NUMBER OF SEQ ID NOS: 20
21 <170> SOFTWARE: PatentIn version 3.3
23 <210> SEQ ID NO: 1
24 <211> LENGTH: 277
25 <212> TYPE: PRT
26 <213> ORGANISM: Homo sapiens
28 <400> SEQUENCE: 1
30 Met Glu Asn Thr Glu Asn Ser Val Asp Ser Lys Ser Ile Lys Asn Leu
31 1               5                   10                  15
34 Glu Pro Lys Ile Ile His Gly Ser Glu Ser Met Asp Ser Gly Ile Ser
35              20                  25                  30
38 Leu Asp Asn Ser Tyr Lys Met Asp Tyr Pro Glu Met Gly Leu Cys Ile
39          35                  40                  45
42 Ile Ile Asn Asn Lys Asn Phe His Lys Ser Thr Gly Met Thr Ser Arg
43      50                  55                  60
46 Ser Gly Thr Asp Val Asp Ala Ala Asn Leu Arg Glu Thr Phe Arg Asn
47 65                  70                  75                  80
50 Leu Lys Tyr Glu Val Arg Asn Lys Asn Asp Leu Thr Arg Glu Glu Ile
51              85                  90                  95
54 Val Glu Leu Met Arg Asp Val Ser Lys Glu Asp His Ser Lys Arg Ser
55              100                 105                 110
58 Ser Phe Val Cys Val Leu Leu Ser His Gly Glu Glu Gly Ile Ile Phe
59          115                 120                 125
62 Gly Thr Asn Gly Pro Val Asp Leu Lys Lys Ile Thr Asn Phe Phe Arg
63      130                 135                 140
66 Gly Asp Arg Cys Arg Ser Leu Thr Gly Lys Pro Lys Leu Phe Ile Ile
67 145                 150                 155                 160
70 Gln Ala Cys Arg Gly Thr Glu Leu Asp Cys Gly Ile Glu Thr Asp Ser
71              165                 170                 175
74 Gly Val Asp Asp Asp Met Ala Cys His Lys Ile Pro Val Asp Ala Asp
75              180                 185                 190
78 Phe Leu Tyr Ala Tyr Ser Thr Ala Pro Gly Tyr Tyr Ser Trp Arg Asn
```

Input Set : A:\25840-501.txt
Output Set: N:\CRF4\09302005\J677977A.raw

```
79          195              200              205
82 Ser Lys Asp Gly Ser Trp Phe Ile Gln Ser Leu Cys Ala Met Leu Lys
83      210              215              220
86 Gln Tyr Ala Asp Lys Leu Glu Phe Met His Ile Leu Thr Arg Val Asn
87 225              230              235              240
90 Arg Lys Val Ala Thr Glu Phe Glu Ser Phe Ser Phe Asp Ala Thr Phe
91              245              250              255
94 His Ala Lys Lys Gln Ile Pro Cys Ile Val Ser Met Leu Thr Lys Glu
95          260              265              270
98 Leu Tyr Phe Tyr His
99          275
102 <210> SEQ ID NO: 2
103 <211> LENGTH: 6
104 <212> TYPE: PRT
105 <213> ORGANISM: Homo sapiens
107 <400> SEQUENCE: 2
109 Phe Ser Phe Asp Ala Thr
110 1               5
113 <210> SEQ ID NO: 3
114 <211> LENGTH: 42
115 <212> TYPE: DNA
116 <213> ORGANISM: Artificial Sequence
118 <220> FEATURE:
119 <223> OTHER INFORMATION: Granzyme B Mutation Forward Primer
121 <400> SEQUENCE: 3
122 ccagcgtata attctaagac agcctccaat gacatcatgc tg                    42
125 <210> SEQ ID NO: 4
126 <211> LENGTH: 6
127 <212> TYPE: PRT
128 <213> ORGANISM: Homo sapiens
130 <400> SEQUENCE: 4
132 Ile Glu Thr Asp Ser Gly
133 1               5
136 <210> SEQ ID NO: 5
137 <211> LENGTH: 42
138 <212> TYPE: DNA
139 <213> ORGANISM: Artificial Sequence
141 <220> FEATURE:
142 <223> OTHER INFORMATION: Granzyme B Mutation Reverse Primer
144 <400> SEQUENCE: 5
145 cagcatgatg tcattggagg ctgtcttaga attatacgct gg                    42
148 <210> SEQ ID NO: 6
149 <211> LENGTH: 6
150 <212> TYPE: PRT
151 <213> ORGANISM: Homo sapiens
154 <220> FEATURE:
155 <221> NAME/KEY: Variant
156 <222> LOCATION: (1)..(1)
157 <223> OTHER INFORMATION: Wherein Xaa is an N-acetyl group.
```

Xaa can only represent a single amino acid, nothing else (see item 13 on Error Summary Sheet)

RAW SEQUENCE LISTING   DATE: 09/30/2005
PATENT APPLICATION: US/10/677,977A   TIME: 12:09:27

Input Set : A:\25840-501.txt
Output Set: N:\CRF4\09302005\J677977A.raw

```
    159 <220> FEATURE:                      same evor
    160 <221> NAME/KEY: Variant
    161 <222> LOCATION: (6)..(6)
    162 <223> OTHER INFORMATION: Wherein Xaa is a 7-amino-4-methylcoumarin group.
    164 <400> SEQUENCE: 6
W--> 166 Xaa Ile Glu Pro Asp Xaa
    167 1                       5
    170 <210> SEQ ID NO: 7
    171 <211> LENGTH: 4
    172 <212> TYPE: PRT
    173 <213> ORGANISM: Homo sapiens
    175 <400> SEQUENCE: 7
    177 Ala Glu Ala Lys
    178 1
    181 <210> SEQ ID NO: 8
    182 <211> LENGTH: 4
    183 <212> TYPE: PRT
    184 <213> ORGANISM: Homo sapiens
    186 <400> SEQUENCE: 8
    188 Glu Asn Val Lys
    189 1
    192 <210> SEQ ID NO: 9
    193 <211> LENGTH: 4
    194 <212> TYPE: PRT
    195 <213> ORGANISM: Homo sapiens
    197 <400> SEQUENCE: 9
    199 Gly Thr Glu Asp
    200 1
    203 <210> SEQ ID NO: 10
    204 <211> LENGTH: 4
    205 <212> TYPE: PRT
    206 <213> ORGANISM: Homo sapiens
    208 <400> SEQUENCE: 10
    210 Ser Pro Thr Arg
    211 1
    214 <210> SEQ ID NO: 11
    215 <211> LENGTH: 4
    216 <212> TYPE: PRT
    217 <213> ORGANISM: Homo sapiens
    219 <400> SEQUENCE: 11
    221 Val Ser Thr Arg
    222 1
    225 <210> SEQ ID NO: 12
    226 <211> LENGTH: 4
    227 <212> TYPE: PRT
    228 <213> ORGANISM: Homo sapiens
    230 <400> SEQUENCE: 12
    232 Ser Thr Ser Phe
    233 1
```

RAW SEQUENCE LISTING   DATE: 09/30/2005
PATENT APPLICATION: US/10/677,977A   TIME: 12:09:27

          Input Set : A:\25840-501.txt
          Output Set: N:\CRF4\09302005\J677977A.raw

236 <210> SEQ ID NO: 13
237 <211> LENGTH: 4
238 <212> TYPE: PRT
239 <213> ORGANISM: Homo sapiens
241 <400> SEQUENCE: 13
243 Lys Phe Pro Asp
244 1
247 <210> SEQ ID NO: 14
248 <211> LENGTH: 4
249 <212> TYPE: PRT
250 <213> ORGANISM: Homo sapiens
252 <400> SEQUENCE: 14
254 Ala Glu Gln Arg
255 1
258 <210> SEQ ID NO: 15
259 <211> LENGTH: 4
260 <212> TYPE: PRT
261 <213> ORGANISM: Homo sapiens
263 <400> SEQUENCE: 15
265 Lys Tyr Ala Asp
266 1
269 <210> SEQ ID NO: 16
270 <211> LENGTH: 4
271 <212> TYPE: PRT
272 <213> ORGANISM: Homo sapiens
274 <400> SEQUENCE: 16
276 Asn Gly Pro Lys
277 1
280 <210> SEQ ID NO: 17
281 <211> LENGTH: 4
282 <212> TYPE: PRT
283 <213> ORGANISM: Homo sapiens
285 <400> SEQUENCE: 17
287 Ser Ser Ala Tyr
288 1
291 <210> SEQ ID NO: 18
292 <211> LENGTH: 4
293 <212> TYPE: PRT
294 <213> ORGANISM: Homo sapiens
296 <400> SEQUENCE: 18
298 Gly Thr Ser Asp
299 1
302 <210> SEQ ID NO: 19
303 <211> LENGTH: 4
304 <212> TYPE: PRT
305 <213> ORGANISM: Homo sapiens
307 <400> SEQUENCE: 19
309 Ala Gln Glu Lys
310 1

Input Set : A:\25840-501.txt
Output Set: N:\CRF4\09302005\J677977A.raw

```
313 <210> SEQ ID NO: 20
314 <211> LENGTH: 4
315 <212> TYPE: PRT
316 <213> ORGANISM: Homo sapiens
318 <400> SEQUENCE: 20
320 Arg Ile Asp Tyr
321 1
```

Input Set : A:\25840-501.txt
Output Set: N:\CRF4\09302005\J677977A.raw

Please Note:
Use of n and/or Xaa have been detected in the Sequence Listing. Please review the
Sequence Listing to ensure that a corresponding explanation is presented in the <220>
to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:6; Xaa Pos. 1,6

VERIFICATION SUMMARY   DATE: 09/30/2005
PATENT APPLICATION: US/10/677,977A TIME: 12:09:28

Input Set : A:\25840-501.txt
Output Set: N:\CRF4\09302005\J677977A.raw

L:166 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:6 after pos.:0